

# Unproven Stem Cell-Based Interventions:

Advancing Policy through Stakeholder Collaboration

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Numerous clinics, in the United States and abroad, have publicized stem cell–based intervention (SCBI) to treat a variety of illnesses and injuries.<sup>1-4</sup> Unfortunately, very few of these published “investigators” have conducted the clinical research necessary to ensure safety and efficacy.<sup>5</sup> Unproven SCBIs pose serious problems for the public and for the field of regenerative medicine itself. These clinics prey on individuals who are desperate for treatments and cures—offering hope to people with autism, human immunodeficiency virus, multiple sclerosis, and Parkinson disease, to cite a few examples.<sup>1,6</sup> Marketing their procedures on websites via videos and testimonials from patients, they play on emotions rather than clinical facts.<sup>3,7</sup> Treatments cost from \$3,500 to more than \$400,000.<sup>5,8</sup>

In the United States, unproven SCBI clinics typically use a patient’s own stem cells, moving cells from one location to another in the body (injecting adipose cells into an injured knee, for instance).<sup>1,9</sup> Using high-quality cells and the optimal dosage for a specific treatment probably leads to the best clinical outcomes.<sup>3</sup> Yet SCBI clinics often do not check the consistency, viability, or number of cells, nor do they use specific biological markers or physical metrics to measure outcomes.<sup>1-3,10</sup> Moreover, they do not perform follow-up evaluations for prolonged periods of time, unless they are trying to get patients to return for regular treatments.

Scientists, regulators, patients, and patient advocates are all stakeholders. But because each perceives the risks, benefits, priorities, and goals differently, each promotes different SCBI practices and policies. To develop an effective policy for SCBIs, stakeholders must collaborate to distinguish between their different perspectives and to reach compromises that best meet competing demands and best respond to the growing number of unproven SCBI clinics.

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## Scientists as Stakeholders

In recent years, many papers and guidelines have been written in an effort to reduce the risks of unproven SCBIs.<sup>11-16</sup> In the absence of reliable preclinical and clinical research, SCBIs should not be used widely. Instead, research should be conducted to advance knowledge and to evaluate the safety and efficacy of new interventions.<sup>2</sup> Allowing unscrupulous clinics to persist can harm the reputation of the field and render more difficult the pursuit of legitimate research to move regenerative medicine forward.<sup>17,18</sup>

Scientists might believe that public education and outreach are the answers. The assumption is that educating patients about the risks of unproven SCBIs will keep them from using these clinics.<sup>19</sup> Although scientists should indeed continue to speak out against inaccurate information, education alone is unlikely to end the application of unproven SCBIs. Education alone has limits to its usefulness, as we have seen in regard to public attitudes toward vaccinations.<sup>20</sup> To shape new policies that minimize the risk both to patients and to research, scientists must also engage policymakers.

## Patients and Patient Advocates as Stakeholders

Many patients pursue these unproven SCBIs because they suffer a debilitating disease or injury and see no alternative.<sup>2,7,21-23</sup> Some patients report positive effects after cell injections, but few data in peer-reviewed journals validate their claims.<sup>24</sup> A few report no change, while others have experienced side effects or death.<sup>5</sup>

Patients tend to judge risks and potential benefits differently than do regulators and scientists.<sup>25</sup> For patients, the risks of unproven SCBIs might seem justified because

they feel they have nothing to lose after exhausting all other options.<sup>19,23,26,27</sup> They are concerned mostly with risks and potential benefits for themselves as individuals, and not with broader applications to later generations. In the absence of miracle cures, even modest improvements are judged worthwhile.<sup>7</sup>

Moreover, patients tend to believe in the power of SCBIs and are excited to see progress in the field.<sup>26</sup> They might think that they are helping to advance treatment by pursuing unproven SCBIs and by sharing their experiences.<sup>26</sup> Furthermore, the excitement surrounding SCBIs—followed by the perceived sluggish pace of science—has left many patients frustrated with scientists and regulators.<sup>2,7,21-23</sup> Patients have been pushing for increased access to potential interventions that are under review by the U.S. Food and Drug Administration (FDA), as well as for new classifications of cell therapies that will make them easier to get on the market.<sup>5,27-29</sup> Patients who are pursuing unproven SCBIs could well be telling us that they have waited long enough for scientists to deliver on their promises.

### Engaging All Stakeholders in Policy Development

Given the risks associated with the increasing number of unregulated SCBI clinics, new FDA policy is warranted.<sup>5,18,30</sup> New research and regulatory strategies must be responsive to the interests and priorities of scientists, regulators, and patients—and to representatives of the clinics that offer unproven SCBIs.<sup>5</sup> Collaboration could yield important insights about what priorities must be met, how they can be met, and which compromises will be acceptable in balancing individual and social interests and needs. The FDA started this process in 2016 by holding discussions with bioethicists, scientists, industry leaders, clinic representatives, and patient advocates.<sup>31</sup> The agency heard feedback on the impact of its proposed rules. New rules have yet to be released, and they are likely to be delayed as we await action by the new FDA Commissioner. Moreover, it is unclear how these guidelines will be affected, given President Trump's executive order that two old regulations need to be removed for every regulation that is added.<sup>32</sup>

Regulatory goals should include protecting the public in the short and long terms by promoting rigorous research while facilitating access to potential therapies. The process should respond to the needs of patients while protecting the public good. Curbing unproven SCBIs requires recognition that different stakeholders are making claims about the appropriate use of unproven SCBIs on the basis of their own values, priorities, and goals.<sup>33</sup> Without facilitating access to rigorously tested therapies and engaging patients, we can expect unproven SCBI clinics to flourish and expand. Without listening to scientists, we are likely to push SCBIs into the market too early—negatively affecting research,

public health, and the long-term potential and hope of regenerative medicine.

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